

# BIOMATERIALS

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## PHASE COMPOSITION OF CERAMIC BASED ON CALCIUM HYDROXYAPATITE POWDERS CONTAINING BYPRODUCTS OF THE SYNTHESIS REACTION

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The formation of the microstructure of ceramic based on the calcium hydroxyapatite (HAP) powders containing different byproducts of the synthesis reaction is examined: NaCl, KCl,  $\text{KCH}_3\text{COO}$  ( $\text{K}_2\text{CO}_3$ ),  $\text{NaCH}_3\text{COO}$  ( $\text{Na}_2\text{CO}_3$ ),  $\text{NH}_4\text{NO}_3$ ,  $\text{NH}_4\text{Cl}$ , and  $\text{NH}_4\text{CH}_3\text{COO}$ , which can be conventionally divided into two groups — substances that can be removed during heat-treatment before sintering starts and substances that cannot be removed, forming melts and promoting the formation of new phases. During heat-treatment sodium salts interact with HAP, forming binary sodium-calcium phosphates  $\text{NaCaPO}_4$  and  $\text{Ca}_{10}\text{Na}(\text{PO}_4)_7$ , and alkali-metal (Na, K) acetates, forming binary carbonates.

**Key words:** ceramic, hydroxyapatite, biomaterials

Ceramic materials based on calcium phosphates are widely used to manufacture bone implants. Such materials can be single-phase or a multiphase composite. Some properties of the materials based on calcium phosphates, for example, solubility, largely depend on the phase composition. The Ca : P ratio (molar) for different calcium phosphates ranges from 0.5 for monocalcium phosphate  $\text{Ca}(\text{H}_2\text{PO}_4)_2$  to 2 for tetracalcium phosphate  $\text{Ca}_4(\text{PO}_4)_2\text{O}$ . Calcium hydroxyapatite (HAP)  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$  with Ca : P = 1.67 exhibits the lowest solubility. As a rule, in monophase materials based on calcium phosphates HAP is a bioresistive phase, i.e., a phase that resists dissolution during implantation. In ceramic composite materials the bioresorbable phases can be represented by calcium-deficient HAP (Ca-DHAP), tricalcium phosphate (TCP)  $\text{Ca}_3(\text{PO}_4)_2$ , calcium pyrophosphate (CPP)  $\text{Ca}_2\text{P}_2\text{O}_7$ , renanite  $\text{NaCaPO}_4$ , double potassium calcium phosphate  $\text{KCaPO}_4$ , calcium carbonate  $\text{CaCO}_3$ , double potassium calcium or sodium potassium carbonates, and glasses in the systems  $\text{CaO} - \text{P}_2\text{O}_5$ ,  $\text{CaO} - \text{P}_2\text{O}_5 - \text{Na}_2\text{O}$ ,  $\text{CaO} - \text{P}_2\text{O}_5 - \text{K}_2\text{O}$ ,  $\text{CaO} - \text{P}_2\text{O}_5 - \text{SiO}_2 - \text{Na}_2\text{O}$ , and  $\text{CaO} - \text{P}_2\text{O}_5 - \text{SiO}_2 - \text{K}_2\text{O}$ . The choice of system for obtaining biocompatible materials based on calcium phosphates is determined by the elements contained in the structure of natural bone.

Powders with high sintering activity must be used to obtain ceramic materials. Consequently, the initial powders for obtaining bioresistive and bioresorbable phases of a composite ceramic material are synthesized by the method of chemical co-precipitation from soluble calcium salts and soluble phosphates. A particularity of synthesis from solutions is that material in the fragmented state is obtained by the condensation (bottom up) method.

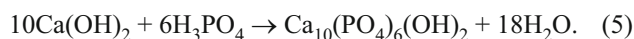
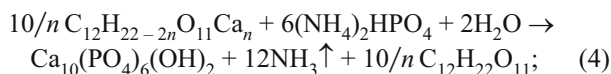
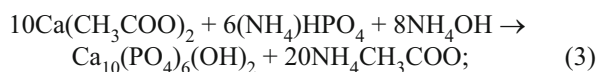
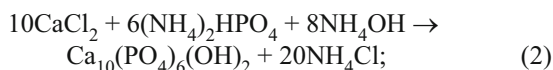
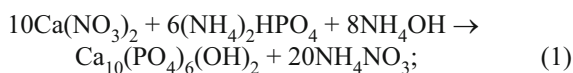
Synthesized target calcium phosphate, for example, HAP, possessing a large specific surface area (at least  $60 \text{ m}^2/\text{g}$ ), adsorbs a substantial (to 35 wt.%) amount of the byproduct of the reaction (BPR), which dissolves easily in water (RF Patent No. 2007119298) [1]. As established previously, the composition and amount of the adsorbed BPR depends on the composition of the mother liquor, which, in turn, depends on the conditions under which synthesis occurs, such as the concentration of the initial solutions and pH. Thus, after synthesis the powder consists of a mixture of calcium phosphate and BPR.

Pairs such as soluble potassium salts and soluble phosphate, which together with the target calcium phosphate form biocompatible BPR or BPR forming when biocompatible phases are calcined, both types of BPR being easily removed on heating, must be used to synthesize highly dispersed cal-

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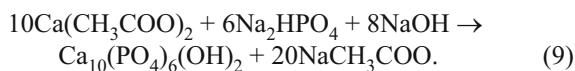
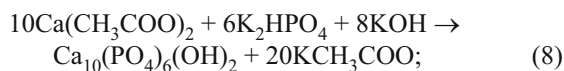
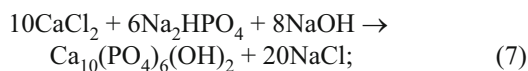
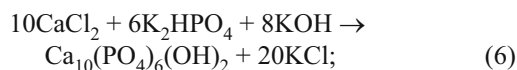
cium phosphate powders for ceramic materials intended for medical use.

The BPR which are removed on heating are formed during the synthesis of calcium phosphate powders from the following precursor pairs: calcium nitrate – ammonium hydrophosphate, calcium chloride – ammonium hydrophosphate, and calcium acetate – ammonium hydrophosphate. The precursor pairs chosen make it possible to synthesize, aside from the target calcium phosphate, BPRs which are removed on heating to sintering (ammonium nitrate, ammonium chloride, and ammonium acetate). The reactions (1) – (5) are used to synthesize HAP powder containing easily removable BPR:



As a result of the reactions (4) and (5), calcium phosphate powders contain removable or nontoxic saccharose or water.

Biocompatible reaction products are formed during synthesis from the following precursor pairs: calcium chloride – potassium hydrophosphate, calcium chloride – sodium hydrophosphate, calcium acetate – potassium hydrophosphate, and calcium acetate – sodium hydrophosphate. The interaction of these precursors results in the formation of, aside from the target calcium phosphate, biocompatible BPR (potassium chloride, sodium chloride, potassium acetate, and sodium acetate):



The reactions (4) – (7) are used to synthesize HAP powder containing biocompatible byproducts of the reactions.

Each of the indicated reactions makes it possible to synthesize HAP, in which incorporation of  $\text{CO}_3^{2-}$  groups, par-

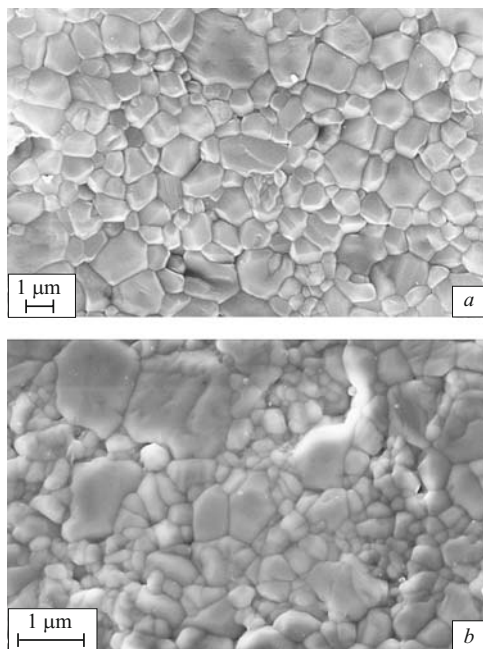
tially replacing phosphate or hydroxide ions, occurs to a lesser or greater degree. Such substitution can have (according to the published data) a positive effect on the sintering of HAP-based materials and does not destroy the biocompatibility of the ceramic materials, increasing somewhat the bioresorbability of HAP. Regulation of the pH of the medium by means of NaOH or KOH, taken in excess, results in a significant presence of  $\text{CO}_3^{2-}$  in the reaction zone and, correspondingly, larger trapping of this ion by the HAP structure with heterovalent substitution of  $\text{Na}^+$  or  $\text{K}^+$  for  $\text{Ca}^{2+}$  at the same time. Such substitutions can intensify the diffusion processes occurring during sintering; this HAP becomes less stable at high temperatures.

Reaction byproducts, including those that are removed on heating, impede aggregation of the primary nanoparticles, separating them, at the storage stage. HAP powder synthesized by co-precipitation from soluble salts has at least a two-level structure; specifically, it consists of aggregates which contain nanocrystals. The size of the primary HAP crystallite, as calculated from XPA data, does not exceed 100 nm. The particle separation by size, obtained by laser diffraction, gives the most likely size of the aggregates 3 to 30  $\mu\text{m}$  after disaggregation. An individual particle (primary aggregate) can be regarded as a nanocomposite, where BPR fulfills the role of a matrix, and the HAP nanocrystallites are distributed in this matrix.

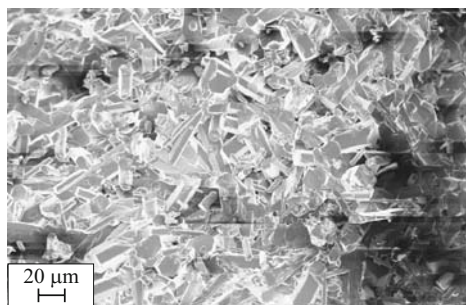
It should be noted that sintering additives are often used in the process of making ceramic materials. This intensifies sintering as a result of the formation of solid solutions or a liquid phase. One condition for the formation of a uniform microstructure is a uniform distribution of the additive introduced. The introduction of a sintering additive in the form of an adsorbed BPR ensures that the additive is uniformly distributed in the powder mass of the HAP synthesized. However, the list of such additives is limited by the requirement of biocompatibility to them and the products formed at high temperature as a result of the interaction of the main phase and the additives.

The reaction (1) is often used to obtain highly dispersed HAP powder. When the pH is kept high (at least 9) the interaction of calcium nitrate and ammonium hydrophosphate makes it possible to obtain a powder that forms, after calcination at 1200°C, a ceramic whose phase composition consists of HAP. In this case, if the pH of the reaction is 6 – 7, after calcination the predominant phase in the material is  $\alpha$ -TCP, and the grain size is smaller. Figure 1a shows that microstructure of a ceramic based on HAP, synthesized at  $\text{pH} > 9$ , after calcination at 1200°C for 6 h, and Fig. 1b shows the microstructure of a ceramic based on Ca-DHAP, synthesized at  $\text{pH} = 7$ , after calcination at 1100°C for 6 h.

The presence of sodium salts (reactions (7) and (9)) in BPR results in the formation of a renanite phase  $\text{NaCaPO}_4$  during calcination. The microstructure of the ceramic made from HAP powder containing a substantial (up to 35 wt.%) amount of NaCl is shown in Fig. 2. The phase composition



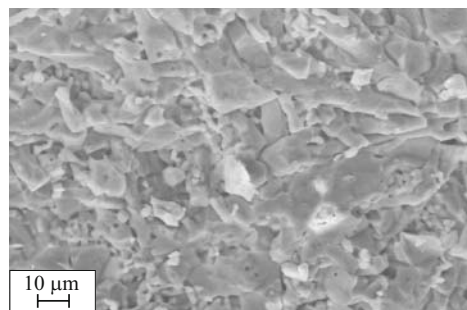
**Fig. 1.** Microstructure of ceramic based on HAP powder (*a*) and Ca-DHAP powder (*b*), synthesized from water solutions of calcium nitrate (0.5M) and ammonium hydrophosphate (0.3M) with Ca : P = 1.67.



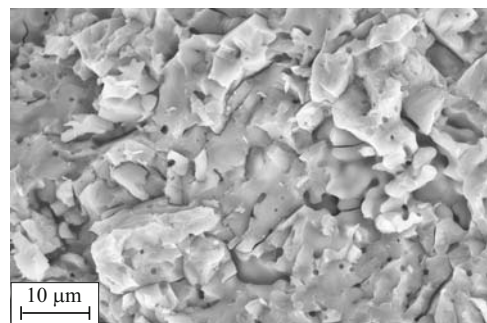
**Fig. 2.** Microstructure of ceramic based on HAP powder synthesized from water solutions of calcium chloride (1M) and sodium hydrophosphate (0.6M) with Ca : P = 1.67 and pH > 9, after calcination at 1200°C for 6 h.

of such a material after calcination at 1200°C for 6 h is represented by  $\beta$ -renanite [5], and the density is not high — the porosity is 50 – 60%. For lower NaCl content the material consists of HAP and  $\beta$ -renanite (Fig. 3). In the synthesis of calcium phosphates via the reaction (9) the pH of the solution does not exceed 8. After calcination at 1100°C for 6 h of HAP samples containing sodium acetate the phase composition of the material is represented by TCP,  $\beta$ -renanite  $\text{NaCaPO}_4$ , and double sodium calcium phosphate  $\text{Ca}_{10}\text{Na}(\text{PO}_4)_7$ . The microstructure of this material is shown in Fig. 4.

The presence of potassium chloride in the BPR composition (reaction (6)) does not lead to the formation, after calcination, of double potassium calcium phosphate. Only a small



**Fig. 3.** Microstructure of ceramic based on HAP powder synthesized from water solutions of calcium chloride (0.25M) and sodium hydrophosphate (0.15M) with Ca : P = 1.67 and pH > 9, after calcination at 1200°C for 6 h.



**Fig. 4.** Microstructure of ceramic based on HAP powder synthesized from water solutions of calcium acetate (0.5M) and sodium hydrophosphate (0.5M) with Ca : P = 1 and pH = 8, after calcination at 1100°C for 6 h.

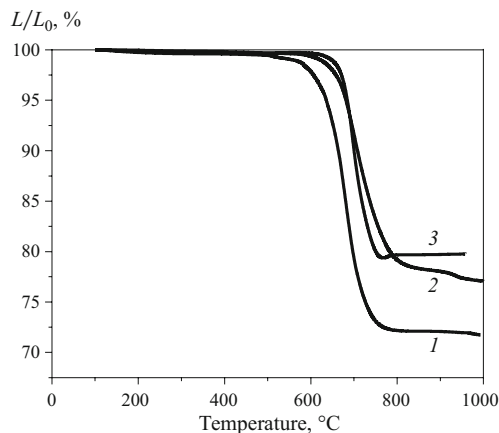
amount chlorapatite is observed. This is probably due to the large ionic radius of the potassium ion, which prevents the formation of double potassium calcium carbonate (sodium calcium).

In the presence of potassium (sodium) acetates in BPR (reactions (8) and (9)), potassium (sodium) or double potassium calcium (sodium calcium) carbonate are formed.

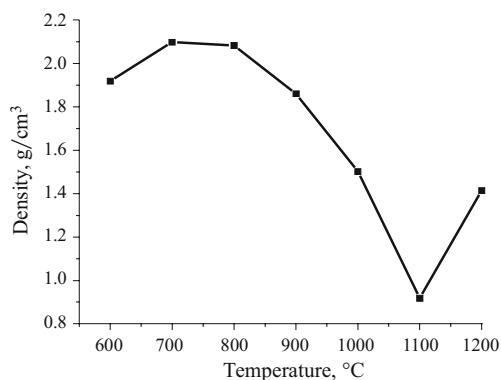
Potassium or sodium chlorides or acetates in BPR substantially lower the densification onset temperature of the material. This is explained by the relatively low melting temperatures of these compounds (295°C for  $\text{KCH}_3\text{COO}$ , 324°C for  $\text{NaCH}_3\text{COO}$ , 776°C for KCl, 801°C for NaCl).

Reaction byproducts can contain NaOH (melting temperature 322°C), KOH (405°C),  $\text{Na}_2\text{CO}_3$  (852°C), or  $\text{K}_2\text{CO}_3$  (894°C), if synthesis occurs in accordance with the reactions (6) – (9). Potassium or sodium carbonates are also formed as a result of the thermal decomposition of acetates. As a result of the presence of these compounds in the powder blank, densification starts at a lower temperature, presumably because of the formation of a melt with a complex composition. Figure 5 shows the dilatometric curves of HAP samples synthesized in accordance with the reaction (7) and containing different amounts of BPR (the main component is NaCl) [2].





**Fig. 5.** Dilatometric curves of HAP samples synthesized from water solutions of calcium chloride and sodium hydrophosphate with different concentrations with Ca : P = 1.67: 1)  $[\text{Ca}^{2+}] : [\text{PO}_4^{3-}] = 0.25\text{M} : 0.15\text{M}$ ; 2)  $[\text{Ca}^{2+}] : [\text{PO}_4^{3-}] = 0.5\text{M} : 0.3\text{M}$ ; 3)  $[\text{Ca}^{2+}] : [\text{PO}_4^{3-}] = 1\text{M} : 0.6\text{M}$ .

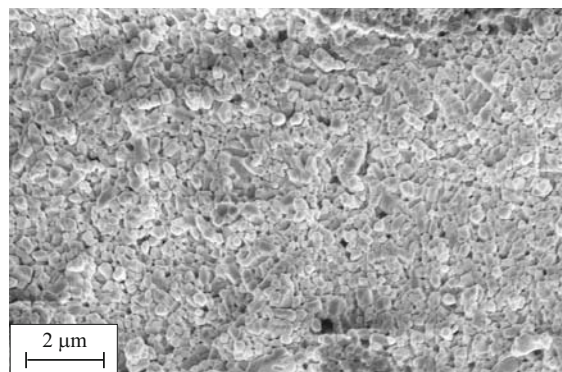


**Fig. 6.** Density versus temperature of HAP samples synthesized from water solutions of calcium acetate (0.5M) and potassium hydrophosphate (0.3M) with Ca : P = 1.67 and pH > 10.

At higher temperatures the carbonates decompose, which in the presence of the melt promotes the formation of porous material. Figure 6 displays the temperature dependence of the HAP samples synthesized via the reaction (6) and containing BPR (the main component is  $\text{KCH}_3\text{COO}$ ) [4].

Figure 7 shows the microstructure of material based on HAP synthesized from calcium acetate and potassium hydrophosphate via the reaction (6), after calcination at 700°C for 6 h (RF Patent No. 2007109483). For calcination at 1100°C for 6 h of ceramic based on HAP synthesized via the reaction (6), the porosity of the material is 70 – 75% (RF Patent No. 2008113835).

In the synthesis of HAP, reaction byproducts such as potassium and sodium chlorides and acetates, hydroxides, and



**Fig. 7.** Microstructure of ceramic based on HAP powder synthesized from water solutions of calcium acetate (0.5M) and potassium hydrophosphate (0.3M) with Ca : P = 1.67 and pH > 10, after calcination at 700°C for 6 h.

carbonates play an important role in the formation of the phase composition of ceramic materials based on calcium phosphates. The presence of these components in a powder blank lowers the sintering onset temperature and the final calcination temperature and promotes the formation of biocompatible and bioresorbable phases.

A substantial part of the BPR, including soluble potassium or sodium acetates and chlorides can be easily removed by repeated washing. However, the small amount of BPR remaining on the surface will modify the surface.

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## REFERENCES

1. T. V. Safronova, M. A. Shekhirev, V. I. Putlyaev, and Yu. D. Tret'yakov, "Ceramic materials based on hydroxyapatite synthesized from solutions with different concentrations of the initial reagents," *Neorg. Mater.*, No. 8, 1005 – 1014 (2007).
2. T. V. Safronova, M. Yu. Steklov, V. I. Putlyaev, and M. A. Shekhirev, "Na-substituted Ca-deficient carbonate hydroxyapatite for obtaining ceramic materials," *Konstr. Kompozit. Mater.*, No. 4, 34 – 39 (2006).
3. T. V. Safronova, M. A. Shiryayev, V. I. Putlyaev, et al., "Ceramic based on hydroxyapatite synthesized from calcium chloride and potassium hydrophosphate," *Steklo Keram.*, No. 2, 23 – 26 (2009).
4. T. V. Safronova, S. A. Korneichuk, V. I. Putlyaev, and O. V. Boitsova, "Ceramics based on calcium hydroxyapatite synthesized from calcium acetate and potassium hydrophosphate," *Steklo Keram.*, No. 4, 28 – 32 (2008).